REMARKS

Substance of Interview

Applicant thanks the Examiner for the telephonic interview of April 1, 2009 with the undersigned and Attorney James Smith. During the interview, Applicant explained that in the device as claimed, a liquid is directed across the fine filter membrane in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis as is recited in independent claims 22, 50, 68, and 69.

Applicant referred to Figure 5, in explaining that the current device has two filters; a rough filter 412 and a fine filter 416. The macromolecule flows perpendicularly to the face of both filters. In context to the claims, Applicant explained that once the macromolecule is pushed through the fine filter 416, the filtered components flow down to waste 518. A buffer is then directed from buffer reservoir 524 across the fine filter (or perpendicularly to the face of the fine filter) in the direction opposite to the direction of the filtration (backwards through the filter). The filtrate on top of fine filter 416 is then pushed to denaturation vessel 526 for further analysis.

In distinguishing Applicant's device from Burshteyn's device (primary reference, U.S. Publication No. 2002/0123154), Applicant explained Burshteyn's Figure 4G. A sample is drawn from the sample container 20 by vacuum 32 into filter device 24. Filter device 24 has side membranes 60. The vacuum further causes filtration of the substance perpendicularly through the side membranes such that only particles of interest remain in the lumen 66 of the filter 24. A buffer 49 is then simply pushed through the lumen 66 (parallel to the filter membranes 60) such the particles of interest are pushed back into sample contain 20.

Applicant explained that if Burshteyn's device worked similarly to Applicant's device, a buffer would be pushed from the region of waste container 39 (for example) through (and perpendicularly to) the membranes 60 in order to push the particles of interest further for analysis. Applicant further explained that this is in contrast to what happens in Burshteyn's device, where a buffer is simply flushed through the lumen 66. Further, in Burshteyn's device, the particles of interest are simply collected in container 20. They are not directed further for analysis to a denaturization vessel as in Applicant's device. Applicant further explained that similarly, secondary reference Sparks (U.S. 6,637,257) also does not describe this step.

The Examiner stated that she would review the filed response and would consider these arguments.

102(e) Rejections

The Examiner has rejected claims 50-54 and 69 under 35 U.S.C. 102(e) as being anticipated by Burshteyn et al. (US Pub. No. 2002/0123154). Reconsideration is requested.

For context, a disclosed embodiment of Applicant's device will first be discussed without limitation of the claims. Applicant's Fig. 5 depicts a schematic of steps that can be included in preparing a macromolecule sample. A rough separation step 410 applies the liquid mixture to a rough filter membrane 412, and a pressure differential across the filter membrane 412 directs at least a portion of the liquid, macromolecule 104, and the fine components 213 through the filter membrane, separating at least a portion of rough components 207 at rough filter 412.

A fine separation step 414 applies the liquid mixture to a fine filter membrane 416, and a pressure differential across the filter membrane directs at least a portion of the liquid and the fine components 213 through the filter membrane to waste 418, separating at least a portion of macromolecule 104 at the filter membrane.

Advantageously, the filters and filtration methods employ the technique of "back-flushing." That is, each filter membrane can be cleaned by directing a fluid, e.g., a buffer, a cleaning fluid, water, a solvent, a desalination buffer, a denaturation buffer, combinations thereof, and the like across the filter membranes in a direction opposite to a previous filtration step. For example, once the macromolecule has gone through the rough filtration step, a liquid can be directed across the rough filter membrane in a direction opposite to the direction of filtration. This cleans the filter membrane surface to restore it to its initial capacity and characteristics. Further, the remaining liquid mixture containing macromolecule 104 can be directed for analysis to denaturation vessel 526.

Burshteyn describes an apparatus and method for removing interferents from a test sample containing a mixture of a composition of interest and interferents in an automated apparatus. As shown in Burshteyn's Figures 2 and 3, the filtration device 24 includes a microporous hollow fiber membrane 60 having a plurality of pores 65 sized to retain the composition of interest while allowing smaller diameter interferents to pass through the

membrane. As shown in Fig. 3, a sample of cells is shown in lumen 66 as a mixture comprising cells 74 and interferents 72. The mean diameter of the pores 65 is smaller than the diameter of the cells of interest, but greater than the diameter of interferents, thus allowing the interferent, to pass through the pores while the cells of interest, or larger diameter cells 74 remain in the lumen 66.

As shown in Figure 4G, a buffer 49 is then dispensed from the buffer reservoir 46 through the filtration device into the sample container 16. Movement of buffer through the device flushes the desired sample of cells from the lumen 66 into the sample container 16.

In response to Applicant's previous arguments, the Examiner points to Burshteyn's Paragraphs 80-85 in saying that "Burshteyn properly reads on the claim language at issue, 'directing a liquid through a filter in a direction opposite to the direction of filtration,' because Burshteyn teaches, in [0082], utilizing a vacuum force to filter the same, then in [0085], the sample is caused to move in an opposite direction that was applied in [0082], which would read on the recited language..." Applicant respectfully disagrees.

In step 80, a vacuum force is applied to pull the sample into the lumen 66 of the filter (Burshteyn, Paragraph 82). It then comes in contact with the tangential filter membranes 60. The sample contacts the filter by being pulled from the sample container up into the lumen 66.

Paragraph 85 states that recovery of the cells from the filter "can be accomplished by providing a force, such as a flow of liquid, to the filter in a direction opposite the direction from which the blood cell sample contacted the filter in step 80." This statement is consistent with every embodiment (not only limited to Figure 3 and 4), where Burshteyn's buffer is directed downward through the lumen from buffer reservoir 46 to simply push the sample into the sample container. It is not directed across the fine filter membrane in a direction opposite to the direction of filtration. If it were, the buffer would be aimed directly through Burshteyn's side membranes 60, and not from the top of lumen to simply flush the sample downward into the sample container.

Further, the flow of Burshteyn's buffer is substantially parallel to the faces of the membranes. In contrast, the flow of Applicant's liquid is directed across or perpendicular to the filter membrane.

Thus, Burshteyn does not describe all the limitations of amended independent claims 50 and 69. Specifically , Burshteyn does not describe directing a liquid across the fine filter membrane in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis . Thus, these claims or any claims dependent on these claims are allowable for at least these reasons.

103(a) Rejections

Claims 22-31, 32-35, 41-43, and 68 have been rejected under 103(a) by the Examiner as being unpatentable over Burshteyn in view of Sparks, U.S. 6,637,257. Reconsideration is requested.

As shown in Sparks' figures 1 and 2, a substrate 12 has micromachined vias 14 that extend through the thickness of the substrate 12. As shown in figures 3 and 4, multiple substrates can be utilized in a single filtering device 10 or 110. The upper most substrate 12 has vias sized to filter relatively large cells or particles, while the middle and lower substrates 12 are sized to filter smaller particles. A manual or automatic back-flushing operation can be performed to remove the cells/particles that have collected at the upstream surface 16 as the need requires (Sparks, col. 6, lines 11-13).

Firstly, one would not look to combine Burshteyn's device with Spark's device. Burshteyn's device is a tangential type filter that is targeted towards filtration of blood cells, where only the larger particles are of interest for analysis. Burshteyn nowhere describes the need to analyze smaller particles. Spark's device is intended to be a multi-phase filtration system for separating larger and smaller particles in steps. Thus, one would not look to combine Burshteyn's one-phase tangential filter with Spark's multi-phase filter.

Further, even if one were to combine these devices, they do not describe directing a liquid across the fine filter membrane in a direction opposite to the direction of filtration, and directing the macromolecule further in the apparatus for analysis as is described by the Applicant. As previously stated, Burshteyn does not describe this limitation. Sparks also does not describe this limitation. Even in Spark's backflushing embodiment, the macromolecule is not directed further for analysis, but is removed.

Thus, neither Sparks nor Burshteyn describe all of the limitations of amended claim 22. Specifically, neither describe directing a liquid across the fine filter membrane in a direction opposite to the direction of filtration, the macromolecule this being directed further in the apparatus for analysis . Therefore, claim 22 or any claim dependent on the same is allowable for at least that reason. Independent claim 68 also recites the same limitation as claim 22 and is thus allowable for the same reasons.

Dependent claim 36 has been rejected as being unpatentable over Burshteyn in view of Holmes (US 4830969). Holmes does not describe any of the limitations of claim 22 that are absent in Burshteyn's and Spark's devices. Thus, dependent claim 36 is allowable over Burshteyn, Sparks, and Holmes either alone or in combination.

Dependent claims 37-40 have also been rejected over Burshteyn in view of Sparks and in further view of Shnipelsky et al (Schnipelsky, US 6645758).

As stated, neither Burshteyn nor Sparks alone or in combination describe all of the limitations of independent claim 22. Similarly, Shnipelsky does not describe any of the limitations of claim 22 that are absent in Spark's or Burshteyn's devices. Dependent claims 37-40 are allowable for at least these reasons.

Also, dependent claim 55 has also been rejected as being unpatentable over Burshteyn in view of Schnipelsky. Shnipelsky either alone or in combination with Burshteyn also does not describe all of the limitations of independent claim 50, on which claim 55 is dependent. Specifically, neither reference describes the step of directing a liquid across the fine filter membrane in a direction opposite to the direction of filtration. Thus, dependent claim 55 is allowable for at least this reason.

CONCLUSION

In view of the above remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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